rapid mobilization of HSCs from niche spaces to peripheral blood. We hypothesize that AMD3100 creates space within the endogenous stem cell niche allowing for better engraftment of transplanted HSC donors.

We found that subcutaneous injections of AMD3100 (5mg/kg) into C57/BL6-Rag2 common gamma chain-deficient mice induced mobilization of HSCs from bone marrow and absolute numbers of HSC in bone marrow reached a nadir four hours post-AMD3100 injection (2013±553 vs. 3765±392, p = 0.02, n = 4-6). AMD3100 pre-treated immunodeficient recipients were transplanted with a bolus dose of 6300 MHC-mismatched AKR/j HSCs. We also performed daily rounds of AMD3100 injections followed by low dose injections of 450 HSCs over the course of 14 days for a total transplant of 6300 cells. HSC bone marrow donor chimerism 12-weeks post-transplant was not increased in the bolus-transplanted animals (1.9±0.6% vs. 1.4±0.3%, p = 0.7, n = 5-9). Repeat-transplanted animals exhibited a slight increase in engraftment; however, this increase was not found to be statically significant (2.1±0.2% vs. 2.5±0.8%, p = 0.4, n = 4-5). These data demonstrate that while AMD3100 is effective as a HSC mobilizer, it is not effective in increasing engraftment potential of transplant recipients.

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USE OF UMBILICAL CORD BLOOD IN TRANSPLANTATION FOR PATIENTS WITH MYELODYSPLASTIC SYNDROME

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Myelodysplastic Syndrome is a clonal hematological disorder characterized by peripheral cytopenias with significant risk for progression to acute myeloid leukemia (AML). It is the most common hematological malignancy in the elderly with 86% of all MDS diagnoses reported in individuals over 60 years of age, according to SEER data. While hypomethylating agents may delay disease progression and extend overall survival in low risk MDS patients, allogeneic hematopoietic stem cell transplant is the only potentially curative therapy for high risk MDS. The use of umbilical cord blood as a stem cell source for MDS patients is attractive because of rapidity of availability as well as the lower risk of GVHD with increasing HLA disparity. Outcomes data is limited, but encouraging results have been reported. This study seeks to examine transplant outcomes of MDS patients receiving umbilical cord blood units from the St. Louis Cord Blood Bank (SLCBB).

As of September 30, 2010, the SLCBB has shipped units for 95 MDS patients, of which outcomes data is available for 46. Summary data is provided in the table below for single and dual cord transplants: Umbilical cord blood is a viable source of stem cells for HSCT in MDS patients. More data will be required to examine a possible risk of increased graft vs. host disease with this population.

Table 1. Data Summary – Single and Dual Cord Blood Transplants

Variable	Single Cord Blood	Dual Cord Blood
N	24	22
Patient Age		
Mean	14.1	44.9
Conditioning Regimen		
Myeloablative	21	9
Non-Myeloablative	3	13
ANC Achieved		
Yes	24 (100%)	19 (86.4%)
No	0 (0%)	3 (13.6%)
Days to ANC Achieved		
Mean	23.3	24.0
Acute GVHD		
Yes	17 (70.8%)	4 (18.2%)
No	7 (29.2%)	6 (27.3%)
Unknown	0 (0%)	12 (54.5%)
Chronic GVHD		
Yes	6 (25%)	1 (4.5%)
No	16 (66.7%)	8 (36.4%)
Unknown	2 (8.3%)	13 (59.1%)
Survival		
Alive	17 (70.8%)	11 (50%)
Expired	7 (29.2%)	11 (50%)
Mean Survival (months)	23.1	11.2

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KILLER-IMMUNOGLOBULIN-LIKE RECEPTOR (KIR) GENE POLYMORPHISM AND BKV ASSOCIATED HEMORRHAGIC CYSTITIS IN HEMATOPOIETIC STEM CELL TRANSPLANT RECIPIENTS

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Hemorrhagic cystitis (HC) is the most prevalent complication of BK viruria after allogeneic hematopoietic stem cell transplantation (HSCT) and is associated with significant morbidity and mortality. However, why 40–50% of HSCT recipients with persistent viruria never develop HC remains unclear. Killer-immunoglobulin-like Receptor (KIR) gene polymorphism has been implicated in influencing clinical outcomes of a number of viruses such as CMV, Hepatitis C, and HIV.

Objective: To determine whether KIR gene polymorphisms has a potential role in the development of BKV associated HC after allogeneic HSCT.

Methods: We performed a retrospective 1:2 matched case-control study of allogeneic HSCT recipients who underwent transplant at our institution from 2000-2010. We performed KIR genotyping for 32 cases with BKV associated HC and 64 matched controls without HC. Two controls were selected for each case, and matched for disease, preparative regimen, and development of acute GvHD prior to HC. Recipient KIR genotyping was determined by PCR-rSSOP (Luminex, One Lambda). Recipient KIR genotype and haplotypes were assigned as described previously (Middleton and Gonzelez, Immunology, 2010). The donor's human leukocyte antigen (HLA) typing was reviewed from patient charts for determination of KIR ligands. Conditional logistic regression analysis was used to assess the association of KIR gene polymorphism and BKV associated HC. Stepwise analysis using a variable entry criterion of $P < 0.10$ and a variable retention criterion of $P < 0.05$ was used to assess multivariable risk factors.

Results: No significant association was identified at the 5% level of significance between the development of HC and KIR genotypes, Haplotypes (AA vs. Bx), number of activating receptors, presence of any particular activating or inhibitory KIRs, or presence of any cognate HLA ligands.

Conclusion: In contrast to the reported associations between KIR gene polymorphism and different outcomes of other viruses, our study does not support a role for KIR gene polymorphism in the development of BKV associated HC.

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WHY WORK-UP REQUESTS FOR HSCT DONORS FAIL – REASONS AND WAYS TO IMPROVE FROM A DONOR CENTER PERSPECTIVE

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Since 1992, DKMS German Bone Marrow Center has processed 28,672 work-up requests for hematopoietic stem cell donations. 4,328 requests (15.1%) were cancelled by the transplant centers for patient-related reasons. Of the remaining, 22,840 (93.8%) requests were successfully completed by collection and transplantation of a viable stem cell product.

Since every work-up is a time and resource intensive process, it is crucial to minimize the number of futile requests. Therefore, we have assessed medical and non-medical conditions leading to donor deferral or temporary unavailability, and identified donor subgroups more likely to cancel their willingness late in the donor search process. Due to the additional costs and loss of time, donors who did

not proceed during and after the medical clearance are of particular interest.

324 donors contacted for work-up (1.3% of the non-cancelled requests) were considered permanently unfit for donation (status DD, *donor deferred*), the majority of them by the apheresis centers during medical clearance. Only 22.8% could be identified by DKMS before apheresis center clearing.

While 828 donors (3.45% of non-cancelled requests) were temporarily unavailable (status TU) for medical or non-medical reasons, the transplant centers could be notified in 61% of those cases prior to medical clearing. 323 donors contacted (1.3% of the non-cancelled) withdrew their consent to donate (32.2% during or after clearance).

We have analyzed demographic factors (age, gender, place of living, ethnicity) to identify potential risk factors for failing work-ups. It showed that 2.0% of female but only 1.1% of male donors withdrew their consent to donate on the work-up level ($p < 0.001$). While the average donor age of all non-cancelled requests was 32.9 years, it was 36.8 years for those donors who were permanently deferred for medical reasons. Medical reasons included both medical findings that were unknown to the donor before physical examination and medical issues known to the donor that could not be covered during confirmatory typing process. The latter category needs to be specifically addressed to further improve the donor selection process.

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OUTCOMES OF A 1-DAY NONMYELOABLATIVE PREPARATIVE REGIMEN FOR PRIMARY GRAFT FAILURE AFTER ALLOGENEIC STEM CELL TRANSPLANTATION

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Primary graft failure after allogeneic stem cell transplantation is a life-threatening complication because of prolonged neutropenia after the initial transplantation. A shortened conditioning regimen followed by re-transplantation may increase the chance of survival. Here, we report 11 patients with a median age of 44 (range, 25-67) years, who received a 1-day reduced-intensity preparative regimen and subsequent re-transplantation for primary graft failure. The diseases in these patients were as follows: acute myelogenous leukemia/myelodysplastic syndromes in 6, myeloproliferative diseases in 3, chronic lymphocytic leukemia in 1, and aplastic anemia in 1. All 11 patients experienced primary engraftment failure following a T-cell depleted, fludarabine-based nonmyeloablative transplantation from a haploidentical donor (n = 6), a matched sibling donor (n = 1), a matched unrelated donor (n = 2), or after myeloablative transplantation from dual umbilical cord blood units (n = 2). The 1-day preparative regimen for graft failure rescue consisted of 30 mg/m^2 fludarabine, 2 g/m^2 cyclophosphamide, 20 mg/body alemtuzumab, and 200 cGy total body irradiation, all delivered 1 day prior to transplantation. Five patients received grafts from the same haploidentical donor; 5, from a different haploidentical donor; and 1, from the same matched sibling donor. Out of the 11 patients, 9 engrafted. Of these, one developed Grade II acute GVHD, and one, Grade I acute GVHD. At present, 8 out of the 11 patients are alive with a median follow-up of 9.2 (range, 2.3-28.8) months from the initial transplantation and 7 are in remission. Three patients died, 1 due to infection and 2 secondary to multi-organ failure. In conclusion, although the number is small, this case-series suggest that our 1-day preparative regimen is feasible, leads to successful engraftment in a high proportion of patients, and might be appropriate for patients requiring immediate re-transplantation after primary graft failure.

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REDUCED INTENSITY VERSUS STANDARD MYELOABLATIVE CONDITIONING IN PATIENTS WITH ACUTE MYELOID LEUKEMIA IN SECOND COMPLETE REMISSION

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Introduction: We have recently presented data for 93 patients (pts) transplanted for AML in CR1 where we did not observe a significant overall survival (OS) difference between reduced intensity (RIC) and myeloablative conditioning (MAC) (5-year OS 61% vs. 56%) despite the fact that RIC pts were significantly older with higher hematopoietic cell transplantation-specific comorbidity index scores (HCT-CI) (Hemmati et al., Int J Hematol. 2010, 91:436-45). Now we aimed to determine whether RIC was similarly safe and effective when administered in CR2.

Methods: We retrospectively analyzed 38 consecutive AML pts who were transplanted in CR2 between 1999 and 2008. 16 pts received RIC (6x30 mg/m2 FLU, 4x4 mg/kg BU, 4x10 mg/kg ATG) and immunosuppression with CSA/MMF and 22 pts received MAC (6x2 Gy TBI and 2x60 mg/kg CY) and CSA/MTX. Donors were HLA-matched related (5/16 vs. 7/22), -matched unrelated (7/16 vs. 12/22) or -mismatched (4/16 vs. 3/22) and peripheral blood stem cells (15/16 vs. 21/22) or bone marrow (1/16 vs. 1/22) were given. Pts in the RIC group were significantly older (58 years (range: 47-69) vs. 39 years (20-57), $p < 0.0001$) and more pts were HCT-CI high risk (7/16 vs. 2/22, $p = 0.02$). All other patient and treatment characteristics were similar.

Results: Median follow-up was 49 months (2-107). OS was significantly inferior for RIC vs. MAC (multivariate HR 2.50, 95%CI: 1.03-6.11, $p = 0.037$) with projected OS rates at 1, 2 and 5 years being 35% vs. 71%, 28% vs. 67% and 28% vs. 52%. Trends for increased cumulative incidence of non-relapse mortality (31% (19% infection, 12% GVHD) vs. 19% (5% infection, 14% GVHD), $p = 0.3$) and of relapse (50% vs. 29%, $p = 0.16$) both contributed to the inferior RIC results. Interestingly, the cumulative incidence of NIH criteria acute (44% vs. 74%, $p = 0.033$) and chronic GVHD (25% vs. 71%, $p = 0.025$) was significantly higher after MAC, suggesting that the lower relapse rate after MAC was not only due to the higher conditioning intensity but also due to a more potent GVL effect.

Conclusions: Although our study population was small and subject to various confounders the current data suggest that in contrast to CR1 FLU/BU/ATG is not an optimal regimen for AML pts in CR2 because non-relapse mortality remains substantial and relapse rates are much higher than with MAC. With reference to the higher incidence of GVHD after MAC we hypothesize that a modification of the RIC regimen with better exploitation of the GVL effect may be beneficial.

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MAJOR ABO MISMATCH INCREASES RED BLOOD CELL TRANSFUSION REQUIREMENTS AFTER ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION USING TOTAL LYMPHOID IRRADIATION AND ANTI-THYMOGLOBULIN CONDITIONING

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Introduction: The clinical impact of ABO mismatch between hematopoietic cell transplant (HCT) recipients and their donors remains controversial. TLI/ATG is a reduced intensity conditioning regimen associated with low rates of non-relapse mortality. Here, we report the effects of ABO mismatch on neutrophil and platelet engraftment, and on red blood cell (RBC) transfusion requirements after TLI/ATG allo-HCT.

Material and Methods: We analyzed the outcomes of 266 patients who underwent TLI-ATG conditioned allo-HCT from Jan 2005 to July 2010, including 139 men and 127 women (median age 57). The most common indications for HCT were acute leukemia (n = 91) and non-Hodgkin lymphoma (n = 73). Cumulative RBC transfusions through 100 days post-HCT, one year post-HCT, and last follow-up were compared between ABO matched and mismatched donor-recipient pairs by the Mann-Whitney test.

Results: ABO matched, major mismatched and bidirectionally mismatched donor-recipient pairs were observed in 141(53%), 54 (20.3%), and 20(7.5%) of cases. In this cohort following conditioning, 149 did not experience an absolute neutrophil count (NC) less than 500/microliter, and 19 patients did not have NC count less